Attorney Docket No.: 47675-042US0 First Applicant's Name: Kurt Berlin

Application Filing Date: 21 April 2005 Office Action Dated: 21 January 2010

Date of Response: 21 July 2010 Examiner: Katherine D. Salmon

IN THE CLAIMS:

Applicants, pursuant to 37 C.F.R. § 1.121, submit the following amendments to the claims:

 (Currently amended) A method for detecting the presence of an a cancer in a particular organ characterized by an increased amount of organ-specific free floating DNA,

comprising:

obtaining a bodily fluid sample from a test human having a cancer in a particular organ

characterized by an increased amount of corresponding organ-specific free floating DNA relative

to that of a normal control value;

measuring an amount or presence of free floating DNA that originates from $\underline{the}[[a]]$

particular organ in the sample comprising analysing for a DNA methylation pattern that is

characteristic for the particular organ; and

comparing the measured amount or presence of free floating DNA that originates from

the particular organ of the test human with that of a normal control value, and determining the

presence of a cancer in the particular organ characterized by an increased amount of organ-

specific free floating DNA based on an increased measured amount of corresponding organ-

specific free floating DNA.

2. (Currently amended) A method for detecting the presence of a cancer <u>in a particular</u>

organ characterized by an increased amount of organ-specific free floating DNA, comprising:

obtaining a bodily fluid sample from a test human having a cancer in a particular organ

characterized by an increased amount of corresponding organ-specific free floating DNA relative

to that of a normal control value;

measuring an amount of total free floating DNA in the sample;

measuring an amount of free floating DNA that originates from a particular organ in the sample comprising analysing for a DNA methylation pattern that is characteristic for the organ;

and

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comparing the total measured amount of free floating DNA and the fraction of free

floating DNA that originates from the organ of the test human, with that of a normal control value, and determining the presence of a cancer in the particular organ characterized by an

increased amount of organ-specific free floating DNA based on an increased fraction of

corresponding organ-specific free floating DNA.

3. (Previously presented) The method of any one of claims 1 and 2, wherein the

sample is treated before the amount or presence of free floating DNA is determined.

4. (Previously presented) The method of claim 3, wherein the sample is treated by at

least one centrifugation, filtering, heating, cooling, concentration and chemical treatment.

5. (Cancelled)

(Previously presented) The method of any one of claims 1 and 2, wherein the 6.

methylation pattern is characteristic for the particular organ and not found in other organs

involved in the cancer characterized by an increased amount of organ-specific free floating DNA

of interest

7. (Cancelled)

(Previously presented) The method of any one of claims 1 and 2, wherein the

sample comprises at least one bodily fluid selected from the group consisting of whole blood.

blood plasma, blood serum, urine, sputum, ejaculate, semen, tears, sweat, saliva, lymph fluid,

bronchial lavage, pleural effusion, peritoneal fluid, meningal fluid, amniotic fluid, glandular

fluid, fine needle aspirates, nipple aspirate fluid, spinal fluid, conjunctival fluid, vaginal fluid,

duodenal juice, pancreatic juice, bile and cerebrospinal fluid.

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(Previously presented) The method of any one of claims 1 and 2, wherein determining the methylation pattern comprises subjecting the DNA to a chemical or enzymatic

treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position 5-

methylated cytosines unmodified.

10. (Currently amended) A method for detecting the presence of a cancer in a

particular organ characterized by an increased amount of organ-specific free floating DNA,

comprising:

obtaining a bodily fluid sample from a test human having a cancer in a particular organ

characterized by an increased amount of corresponding organ-specific free floating DNA relative

to that of a normal control value;

measuring an amount or presence of free floating DNA that exhibits a DNA methylation

pattern characteristic of a particular organ;

determining, based on the measuring, whether there is an increased level, relative to that

of a control value, of free floating DNA that originates from the organ; and

determining, based on finding an increased level of free floating DNA that originates

from the organ of the test human, a presence of a cancer in the particular organ characterized by

an increased amount of corresponding organ-specific free floating DNA.

(Currently amended) A method for detecting the presence of a cancer in a

particular organ characterized by an increased amount of organ-specific free floating DNA,

comprising:

obtaining a bodily fluid sample from a test human having a cancer in a particular organ

characterized by an increased amount of corresponding organ-specific free floating DNA relative

to that of a normal control value;

measuring an amount of total free floating DNA in the sample;

measuring an amount of free floating DNA that originates from a specific organ by

determining an amount of free floating DNA that exhibits a DNA methylation pattern

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characteristic of the organ;

determining the fraction of total free floating DNA that originates from the specific organ;

determining whether an increased fraction, relative to that of a normal control value of free floating DNA that originates from the specific organ is present; and

determining, based on finding an increased fraction of free floating DNA that originates from the organ of the test human, the presence of a cancer in the particular organ characterized by an increased amount of corresponding organ-specific free floating DNA.

 (Previously presented) A method for determining the fraction of total free floating DNA in a bodily fluid that originates from a specific organ, comprising:

obtaining a bodily fluid sample of a test human;

conditioning the sample to provide for binding of total free floating DNA to a surface;

binding an amount of the total free floating DNA to the surface;

detecting an amount of total free floating DNA by measuring the amount of DNA bound to the surface;

subjecting the surface comprising the bound DNA to at least one of a chemical and enzymatic treatment that converts all unmethylated cytosines in the DNA into uracil but leaves position-5 methylated cytosines unmodified:

amplifying the treated DNA;

analysing several methylation-specific positions in the treated DNA, and thereby determining an amount of DNA that exhibits an organ-specific DNA methylation pattern; and

comparing the amount of DNA that exhibits an organ-specific DNA methylation pattern to the amount of detected total free floating DNA, thereby determining the fraction of free floating DNA that originates from the specific organ in the total free floating DNA.

(Previously presented) The method of claim 12, further comprising:
determining whether an increased level of free floating DNA that originates from the

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specific organ is present; and

determining the presence of a cancer in a particular organ characterized by an increased

amount of organ-specific free floating DNA, based on comparing the presence of such an

increased level of free floating DNA that originates from the particular organ of the test human,

with that of a normal control value.

14. (Previously presented) The method of any one of claims 1, 2, 10, 11, 12 and 13,

wherein measuring the total amount of free floating DNA comprises use of at least one means

selected from the group consisting of: intercalating fluorescent dyes or other dyes exhibiting

changing fluorescence properties upon binding to DNA; hybridisation to DNA specific

oligonucleotide or PNA oligomer probes; real time PCR assays; real time amplification

procedures; UV-Vis absorbance; and amplification procedures with subsequent determination of

the amount of product amplificate formed.

15. (Cancelled)

16. (Cancelled)

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